TV

Drug Trials—the Dark Side: This World

BBC1, 27 April at 9 pm

Rating: ★★★★

An advert posted inside some London buses shrieks, "Drop by today—it could be a beneficial visit!" Placed by the pharmaceutical services company PAREXEL, it seeks volunteers for research—at Northwick Park Hospital. The recent disastrous trial of the monoclonal antibody TGN 1412 at that venue has heightened the public's interest in clinical drug studies. And the long term result may be increased scepticism, such that fewer people in the United Kingdom will be willing to participate in clinical research, no matter how upbeat the recruitment messages.

In addressing this problem, the pharmaceutical industry is, predictably, well ahead of the game. For instance, clinical trials are increasingly being conducted in developing countries that offer a rich source of suitable and apparently willing patients. *Drug Trials—the Dark Side* was a compelling documentary on how drug companies are targeting India for this purpose.

The scene was set by the comments of a patient-recruitment agent, who boasted how much quicker and cheaper it was to enrol patients for trials in India, compared with, for example, the United States and countries in western Europe. He also emphasised how India had a huge supply of "treatment-naive" people, or in the words of Paul Kenyon, the programme's presenter, "patients offering a blank canvas to the drug companies." From this starting point, Kenyon set out to discover just why so many people are ready to take part in clinical studies, even though they receive no financial reward.

Through interviews, case studies, and on the spot reporting, Kenyon showed how the rapid recruitment commonly relies on insufficient regard for ensuring that patients give informed consent. This abuse of a fundamental principle of research in humans can be attributed largely to a poisonous combination of four factors: ill health, poverty, ignorance, and blind faith in the medical profession. Patients too poor to afford standard therapy, and with little or no understanding of clinical research, are only too happy to accept what appears to be "free" treatment from doctors they revere.

In such circumstances, the notion of truly informed and freely given consent becomes highly questionable, as the documentary made clear. And it was easy to sympathise with the consultant who dismissed as a myth the idea that such consent was possible where patients felt so obligated to their doctors and would consequently "agree" to anything they were asked to do. Acting on his ethical objections, this doctor had taken a brave, atypical stand in refusing to allow trials in his hospital. Others are not so fastidious, seemingly wary of ostracism by colleagues and frightened of upsetting the drug companies.

Testimony to how little some patients really knew was their thumbprints (rather than signatures) on consent forms written in English, a foreign language. Of particular concern were examples of where patients' supposedly informed consent to take part in trials had meant that essential treatment had been delayed or stopped in favour of untested interventions.

There was a particularly eye-opening demonstration of failure to inform a potential trial participant. In an unusual move, one drug company allowed Kenyon to film the recruitment of a patient to a study of a drug for rheumatoid arthritis. Even in this heavily stage-managed setting (where the film crew could not arrive unannounced) and despite the well meaning efforts of the recruiting doctor, it was obvious that the patient had "consented" to enter the (placebo controlled) trial without really knowing he was agreeing to an experiment. More worrying still, he appeared to believe that the treatment would cure his arthritis, an assumption apparently unchallenged during the consent-seeking process.

Whatever the faults in how participants are recruited, the boom in India's clinical trial industry is set to continue. Indeed, drug companies may become ever more dependent on carrying out research on compliant patients in developing countries, to help minimise the cost of acquiring data needed for the licensing of new medicines.

BBC

Parshottam Parmar: "I didn't know that experiments were being carried out on me"

What is more, Western countries may find it convenient to have such treatments tested elsewhere, especially if this obviates TGN 1412-type incidents on their own doorstep. *Drug Trials—the Dark Side* should help to ensure that such delegation of risk does not blind us to the costs borne on our behalf by others far away. Crucially, the programme also highlighted how in India at least, taking part in a trial does not guarantee subsequent affordable access to the tested medicines, even for the study patients, let alone the population in general. This is a pointed corrective to any suggestion that unknowing participation in a study might be justifiable if it is the only means of access to "free" treatment.

One final point: randomised clinical trials are often called the "gold standard of medical research." Overuse of this intellectually sloppy phrase has much to answer for. In particular, it can mean that trials are too often considered intrinsically worthwhile, with too little attention being paid to whether, where, and how they should be conducted. To help foster such scrutiny, it is better to view clinical studies as the least bad way available of answering certain health care questions. Sometimes, as Kenyon's important film showed, they are not even that.

Ike Iheanacho *editor, Drug and Therapeutics Bulletin*
Ike.Iheanacho@which.co.uk

Items reviewed are rated on a 4 star scale (4=excellent)

FILM

Indian film-maker tackles hypochondriasis

Shaadi se Pehle: a film in Hindi
now showing in cinemas in India
Directed by Satish Kaushik
Written by Sanjay Chhel
www.shaadisepehle.com

Rating: ★★★☆

A film currently showing in India deals with an often ignored but growing health issue in the country—hypochondriasis. *Shaadi se Pehle* (which means "before the marriage" in Hindi) depicts the havoc that the condition can cause in the life of a successful businessman. Aashish Kapoor (elegantly played by Indian actor Akshaye Khanna) is a talented advertising executive, well known for coming up with creative ideas at the agency where he works. But, despite doing so well professionally, he constantly feels unwell even though he has no obvious illness. His hypochondriasis and constant concerns about his health gradually start to change his life. He tries a range of different medicines and his behaviour changes to that of someone who is sick.

Despite consulting a doctor who confirms that he's perfectly healthy, Kapoor remains unconvinced. Things escalate still further when he overhears the doctor making a phone call about another patient and mistakenly thinks it is about him, so starts believing that he has end-stage cancer. Fearing that he hasn't got much longer to live, the now very depressed man decides to leave his girlfriend, even though he loves her deeply, so that she can have a better life. His life sinks into a trough of depression, dominated by thoughts about death.

But—as in all good Bollywood films—there is a happy ending. Kapoor is eventually convinced by his doctor that he does not have cancer. He realises that his negative thoughts are making him ill and acts on his doctor's advice: "Think positively, live life." In true romantic style, he regains his girlfriend's love.

"Think positively, live life"

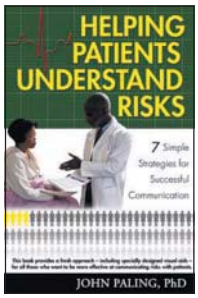
In a relatively poor, developing country such as India, people pay less importance to psychiatric conditions than to physical illnesses. Psychiatric problems are now increasing sharply and there have been a large number of suicides in recent years. It has been projected that developing countries will suffer a major increase in the burden of mental illness over the next two decades. Hypochondriasis—defined as a persistent, non-delusional preoccupation with fears of having severe physical disease despite appropriate medical evaluation and reassurance—may seem relatively minor, but it can seriously impair patients' quality of life. It may also be associated with other psychiatric disorders and so should not be ignored.

Shaadi se Pehle wraps up some useful factual information about hypochondriasis in a humorous format. Apart from some cinematic exaggeration in places, the film accurately portrays the "nitty-gritty" of the condition from an Indian perspective. Films are considered a powerful medium for mass communication in India, so Kapoor's story should improve public awareness about hypochondriasis. It also reminds health professionals of the need to look out for, and help patients to manage, this common but overlooked condition.

Sanjit Bagchi
private medical practitioner and medical journalist, Calcutta, India
drsanjitbagchi@rediffmail.com

Helping Patients Understand Risks: 7 Simple Strategies for Successful Communication

John Paling



Risk Communication Institute,
$29.95 plus postage, pp 208
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www.riskcomm.com/hpur.htm

Rating: ★★★☆

Hands up if you skipped epidemiology and statistics lectures when you were a student. Struggle with maths homework? Still think you have a realistic chance when you buy a lottery ticket? Many doctors are uncomfortable with numbers and, unless you are interested in horse racing, greyhounds, or cards, it is difficult to fully understand risk, chance, and the odds of success. But our patients want to know the likelihood of success in an operation, the benefits and risks of a drug, or the likelihood of developing a disease. And we need to be able to communicate that risk to patients.

If you work with alligators, you know about risk. As a former wildlife film maker, the author has a background in communication. This helps, because communication is often a medical weak spot. The author knows this and tries to give us the appropriate tools to explain.

Numbers are simple. It is our interpretation that makes them difficult. Mistakes happen and medical litigation is littered with the hazards of misunderstood or misread drug doses. Simple numbers can be misinterpreted and even basic concepts can be difficult. For example, some may perceive the risk of one in 250 as greater than one in 25, simply because they see only the larger number.

Communication is complicated. People see and hear what they wish. Words only take meaning after we put them through our emotional filter, and this process can cause much inaccuracy, confusion, injury, and hurt. What patients see and hear is coloured by their individual and family experience and by the expectations of society. In a difficult emotional consultation about prognosis in serious illness, patients easily misunderstand risk. If we had a simple means to explain risk—a visual aid, an illustration, or a practical example—it would be so much easier.

John Paling, building on his media experience, shows us how to use charts and scales. His own patented model is a "Palette" of a thousand figures. Using one thousand as the common denominator, together with the author's charts, scales and palettes, makes it easier to illustrate chance, clarify relative and absolute risk, and provide a model to compare risk across many aspects of life.

Domhnall MacAuley *general practitioner, Belfast*
domhnall.macauley@ntlworld.com

PERSONAL VIEW

A way out for the conscientious objector: "become" a mental patient

Military service for a period of two to three years is compulsory for everyone in Israel. Male doctors, in common with other male citizens, have to serve in the army reserves for periods of up to two months each year until the age of 51. They therefore face situations during their professional lives that colleagues in countries without compulsory military service do not, fortunately, encounter.

In a country such as Israel, military service is seen as a reflection of a person's involvement with their community. Being unwilling to serve can have major implications on someone's future, including their job prospects and practical issues such as obtaining a driving license.

Psychiatrists are regularly required to assess people whose chief complaint is reluctance to serve in the army. Some of these people justify their position on personal grounds, such as job or family commitments, or tiredness resulting from the harsh realities of policing the Israeli occupation of the Palestinian territories and population.

Refusing to serve in the army on ideological grounds is difficult

Refusing to serve in the army simply on ideological grounds is difficult. Those who try this route have to endure long periods in prison before being recognised as conscientious objectors, according to cases documented by human rights organisations.

One way out for conscientious objectors is to be diagnosed with a psychiatric illness. In my experience as a psychiatrist doing reserve military service, many soldiers choose this path to apply for discharge. The almost daily scenario facing a psychiatrist is a soldier who is left with no other choice than "becoming" a mental patient. This means that, as long as the psychiatrist understands the soldier's predicament, what follows is an effort to medicalise the problem. Reluctance to serve in the army is subsequently re-categorised as an outcome of anxiety, mood disorder, personality disorder, or impulse control disorder, or given some other mental illness diagnosis.

Am I casting doubt on the professional competence or integrity of my colleagues in Israel? No. There are some clear cases of psychopathology where the obvious outcome is discharge from the army. However, the issue becomes more complex during periods of increased conscription, when the divisions between active avoidance, passive refusal, and silent protest become blurred.

This problem occurs, in my opinion, when there is a lack of complete consensus in a society about the perceived righteousness of a war in which it is fighting. The consensus in Israel has been incomplete since the highly unpopular war against Lebanon.

In 2002 when Jenin and other cities on the West Bank were destroyed, it was impossible not to empathise with the plight of soldiers requesting psychiatric assessment, who claimed they had strong grounds on the basis of personal or family problems for not serving. Although most of them would have disagreed that they were conscientious objectors, I asked myself repeatedly about the extent to which these soldiers were reflecting the profound distress pervading Israeli society more generally. I also questioned why psychiatrists ended up with the task of medicalising human suffering and diagnosing people as being mentally ill when their main symptom was that they wanted to live and let live.

This situation poses a moral and ethical dilemma. But it could easily be dealt with by disentangling the "social" from the "medical." The problem is that refusal to serve is seen as a problem with "motivation," which is neither ideological nor mental. Because the Israeli army—along with armies in most Western countries—is reluctant to recognise refusal to serve because of pacifist views or objection on the grounds of conscience, no one takes responsibility for dealing with the issue.

Some Western countries, including France and Germany, have long recognised conscientious objection as a reason for refusing to enlist. And some of the countries in the former Soviet bloc, notably Poland, followed this path during the 1990s. But in countries where conscientious objection is not seen as a valid reason for reluctance to serve in the army, soldiers continue to suffer. The psychiatrist, in turn, is pressed between his loyalty to the soldier-patient's welfare and pressure from the army.

The soldier's fate will depend on the individual psychiatrist's views on values and human rights. On many occasions, empathising with a fellow human being in distress, I simply tried to do everything possible to negotiate their discharge.

Psychiatrists constantly face moral and ethical dilemmas rooted in social suffering. We need to understand the social and political context of situations if we want to give effective help. We all have a duty to protect and preserve life. Ultimately, both soldiers and civilians are victims.

Daniel Moldavsky *consultant psychiatrist, Sittingbourne, Kent*
daniel.moldavsky@icc.wkentmht.nhs.uk

SOUNDINGS

Glimpses of the past

Immersed in the story as I was while listening in the car on the way to work, I found myself wondering about what would happen to Mary Thorne. Was Frank Gresham going to propose or would he "marry money"? Would Mary herself give him up? I had long forgotten how it all ended, and listening to one episode at a time I felt each morning rather like Charles Dickens' readers, who would excitedly wait at the wharf in New York for the ship bringing the next episode of *David Copperfield*.

Doctor Thorne (1858) is Anthony Trollope's third Barchester chronicle, still read and relevant when so many once fashionable authors have sunk into oblivion. Marrying money and preserving distinctions of rank and blood are the predominant themes, but the book should also interest doctors, especially those discontented with present day arrangements.

Trollope's hero, Doctor Thorne, charges only seven shillings and sixpence for a visit and supplements his income by dispensing medicines that he himself mixes up. His rivals, or indeed enemies, are the fashionable Barchestesr physicians who charge several guineas and look down with contempt on the apothecary. Medical practice consists of calling at patients' houses, on a horse or in a horse carriage. Prescriptions are written for drugs that we may safely infer were mostly ineffective and sometimes harmful. When things get sticky the solution is to call in another doctor in consultation. The fashionable physicians will have nothing to do with their apothecary rival, but may on occasion call in a famous physician from London. Some patients are notoriously fickle, now calling in Dr Thorne, now his rivals.

The doctors' armamentarium is clearly limited. But they make up for this by spending much time with the patient, even staying all night if the patient is very ill or dying, especially if the patient is wealthy or important. The fashionable doctors write reports for a medical gazette. Dr Thorne manages the squire's money and gives sensible lifestyle advice.

An often quoted passage explains how to collect a fee without embarrassment. It should be done without a look, without a move of the facial muscles, with hardly an awareness "that the last friendly grasp has been made so much more precious by the touch of gold." How much easier to receive a monthly pay cheque.

George Dunea *attending physician, Cook County Hospital, Chicago, USA*